Chemical Science



EDGE ARTICLE

View Article Online
View Journal | View Issue



Cite this: Chem. Sci., 2021, 12, 15719

d All publication charges for this article have been paid for by the Royal Society of Chemistry

Received 1st November 2021 Accepted 19th November 2021

DOI: 10.1039/d1sc06038d

rsc.li/chemical-science

Direct synthesis and applications of solid silylzinc reagents†

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The increased synthetic utility of organosilanes has motivated researchers to develop milder and more practical synthetic methods. Silylzinc reagents, which are typically the most functional group tolerant, are notoriously difficult to synthesize because they are obtained by a pyrophoric reaction of silyllithium, particularly Me₃SiLi which is itself prepared by the reaction of MeLi and disilane. Furthermore, the dissolved LiCl in silylzinc may have a detrimental effect. A synthetic method that can avoid silyllithium and involves a direct synthesis of silylzinc reagents from silyl halides is arguably the simplest and most economical strategy. We describe, for the first time, the direct synthesis of PhMe₂SiZnI and Me₃SiZnI reagents by employing a coordinating TMEDA ligand, as well as single crystal XRD structures. Importantly, they can be obtained as solids and stored for longer periods at 4 °C. We also demonstrate their significance in cross-coupling of various free alkyl/aryl/alkenyl carboxylic acids with broader functional group tolerance and API derivatives. The general applicability and efficiency of solid Me₃SiZnI are shown in a wide variety of reactions including alkylation, arylation, allylation, 1,4-addition, acylation and more

Introduction

Organosilicon compounds are widely utilized in various disciplines¹ and employed in a broad range of organic transformations.² Traditional silylating agents include silanes (R₃SiH),²a,h disilanes,²f,l,3 silylboranes,²c,4 electrophilic silyl halides and nucleophilic silyl anions (Fig. 1a). While silanes are extensively utilized in hydrosilylations,²h,5 silyl halides are usually combined with organometallic reagents to forge C–Si bonds. Noteworthy examples are the recently developed silyl-Negishi and cross-electrophile coupling reactions by Watson6 and Shu7 and co-workers. The complementary silyl anions are also well established, and silylzinc reagents in general are one of the most appealing8 owing to their excellent functional group tolerance. Earlier in 1984, Oshima et al. described the synthesis of silylzinc reagents,9 and Oestreich and co-workers followed up with elegant applications.¹0

However, it is notoriously difficult to synthesize silylzinc reagents because it requires the preparation of silyllithium reagents.¹¹ In particular, preparation of Me₃SiLi necessitates treating MeLi with hexamethyldisilane in HMPA, evincing the remarkably high activation barrier required for effecting Si–X

School of Chemistry, Indian Institute of Science Education and Research Thiruvananthapuram, Vithura, Thiruvananthapuram, Kerala 695551, India. E-mail: rr@iisertvm.ac.in cleavage. Furthermore, the application of these reagents may be limited due to the dissolved lithium halides. The direct synthesis of silylzinc reagents is undoubtedly a desirable and economical route for the synthesis of silylzinc reagents, as it avoids the handling of pyrophoric silyllithium. Additional benefits may be obtained if the reagents are accessible as solids. Despite the fact that considerable advances have been made in the preparation of organozinc reagents, particularly by

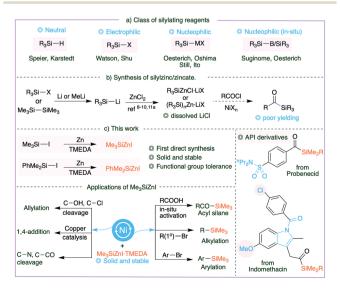


Fig. 1 Synthesis of silylzinc reagents and acylsilanes.

 $[\]dagger$ Electronic supplementary information (ESI) available. CCDC 2089058 and 2089062. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/d1sc06038d

following Knochel's protocols, 12 the existing methods are not amenable to the synthesis of silylzinc reagents through reductive metalation of zinc to silyl halides.

Acylsilanes, on the other hand, are versatile and unique building blocks in organic synthesis.13 They undergo a broad range of reactions including nucleophilic addition,14 transitionmetal mediated reactions¹⁵ and intriguing transformations.¹⁶ Importantly they have been utilized as acyl anion synthetic equivalents via the Brook rearrangement. 13d,f,14d,15a,17 It is ideal to employ carboxylic acid derivatives to synthesize acylsilanes; indeed, stoichiometric organosilicon reagents18 or disilanes19 or stannylsilanes²⁰ in the presence of catalytic palladium at 110 °C have been employed to synthesize acylsilanes. Despite the initial achievements, the synthesis of acylsilanes still involves a tedious protocol, as seen by the contemporary literature that uses the classical multistep 1,3-dithiane protocol,21 or inconvenient protocols. 16a Our attempts to couple silvlzing (prepared from silyllithium) and acid chlorides yielded poor results, perhaps owing to the dissolved LiCl, emphasizing the need for a new and facile synthetic strategy.

Herein we describe the first direct preparation of silylzinc reagents from silyl iodides and subsequent cross-coupling reactions with *in situ* prepared acid chlorides to generate a library of acylsilanes with broad functional group tolerance. In addition, the newly developed solid Me₃SiZnI was successfully employed in a broad range of organic transformations including alkylation, arylation, allylation, 1,4-addition, acylation, cross-coupling *via* C–N bond cleavage, Brook rearrangement and decarboxylation.

Results and discussion

We began our studies with silyl iodide 1a which was prepared from the corresponding PhMe₂SiH.^{6,22} It has been reported in the literature that the activation of zinc is crucial and there are multiple methods known for the activation of zinc²³ including HCl wash,24 Me₃SiCl,25 iodine,26 ultrasound27 and dibromoethane activation.28 We have also followed these protocols for the activation of zinc and subjected them to reductive metalation to silyl iodide 1a, and the results are summarized in Table 1. As expected, no silylation was observed in the absence of an activator or additive (entry 1). Initially, activation was carried out with Me₃SiCl (entries 2 and 5); later iodine (entries 3 and 6-8) and DBE (entry 5) were employed to activate Zn. In general, THF was not suitable (entries 1, 2, and 5), and the C-O bond in THF was cleaved under reflux conditions (Fig. 1 and S5-S7 in the ESI†); a similar observation was reported during the synthesis of silylmagnesium reagents.29 The group of Knochel extensively studied the role of LiCl in the preparation of organometallic reagents including organozinc reagents.12 The same group reported the combination of LiCl, dibromoethane and Me₃SiCl which is highly efficient for the preparation of alkyl zinc reagents. 12e Unfortunately, the inclusion of LiCl as an additive or DBE as an activator was inconsequential (entries 4 and 5).

In the backdrop of our recent findings on the preparation of Me_3SiMgI from Me_3SiI^{30} and the literature reports on polar solvents such as dimethylacetamide, 26,31

Table 1 Synthesis of silylzinc reagents^a

PhMe ₂ Si—I	Zn (2 eq.) activator/additive solvent (1.2 M)	PhMe ₂ Si-ZnI	Me ₃ Si-ZnI
1a		2a	0.56 M 2b

Entry	Activator	Additive, solvent, temperature	2a (M)
1	_	THF, 60 °C	ND
2	TMSCl	THF, 60 °C/toluene, 70 °C	ND
3	Iodine	DMA, 80 °C/toluene, 70 °C	ND
4	_	LiCl, toluene, 70 °C	ND
5	DBE	LiCl, toluene, 70 °C/THF, 60 °C	ND^b
6	Iodine	TMEDA, toluene, 66 °C, 63 h	0.21
7	Iodine	TMEDA, toluene, 70–90 °C, 63 h	0.68^{c}
8	Iodine	NMP/DMA, toluene, 85 °C	ND

^a Reaction conditions: additive/activator: Me₃SiCl (0.12 eq.), iodine (0.03/0.05 eq.), DBE (0.03 eq.), LiCl (1.0 eq.), TMEDA (1.1 eq.), NMP/DMA (1.5 eq.). ^b Me₃SiCl (1.5 mol%) was used. ^c An average of 5 isolated runs. M: molarity, DBE: 1,2-dibromoethane, NMP: N-methyl-2-pyrrolidone, DMA: dimethylacetamide, ND: not detected.

N,N-dimethylformamide, 26,27,31 hexamethylphosphoramide,³² dimethylsulfoxide,32 acetonitrile,33 tetramethylurea,27a CH3CNpyridine³³ and N-methyl-2-pyrrolidone (NMP^{27a}) favoring the generation of organozinc reagents, we envisioned that amine additives may assist the formation of silylzinc reagents. Pleasingly, we observed a successful reductive metalation of zinc when an industrially friendly solvent,34 toluene, along with 1.1 eq. of TMEDA was employed as an additive (entry 6). An increase in the reaction temperature also increased the concentration of PhMe₂SiZnI (entry 6 vs. 7). As shown in entry 8, no reactivity was observed with either NMP or DMA as additives. The methodology is not limited to the synthesis of PhMe2SiZnI 2a; even the relatively less reactive Me₃SiI was successfully employed to generate more productive Me₃SiZnI 2b with 0.56 M (average of 4 runs) concentration. Attempts to synthesize Et₃SiZnI from Et₃SiI were made, and although a concentration of 0.16 M was obtained for Et₃SiZnI, subsequent application utilizing Et₃SiZnI was unsuccessful. Using Me₃SiBr instead of Me₃SiI was likewise unsuccessful, and a poor concentration of 0.04 M was observed. Moreover, these silylzinc reagents (in toluene) stored at 4 °C did not decompose even after six months. Importantly, we obtained the structures of PhMe₂SiZnI·TMEDA and Me₃SiZnI·TMEDA from single crystal XRD for the first time (Fig. 2). It is apparent from these structures that TMEDA stabilizes 2a and 2b, the driving force for the reductive metalation.

At the outset of our studies, we screened a range of nickel catalysts to obtain the acylsilane **5a** (see ESI S11 and S12† for complete tables). The initial experiments were carried out with the isolated acid chloride **4a** derived from 3-(4-methoxyphenyl) propanoic acid **3a**; however, the later experiments (entries 8–16 and 20) were carried out with free carboxylic acid **3a** *via in situ* generation of acid chloride **4a**. When 10 mol% of NiBr₂·diglyme was employed, we observed 60% of the cross-coupling product **5a** (entry 1, Table 2). The yield of **5a** was greatly improved by increasing the reaction temperature from 45 °C to 60 °C (entry 1

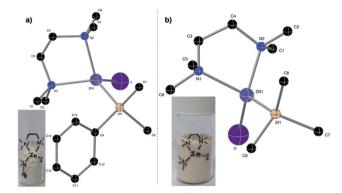


Fig. 2 X-ray crystal structures of (a) PhMe₂SiZnI·TMEDA and (b) Me₃SiZnI·TMEDA complexes; the hydrogen atoms have been omitted for clarity.

vs. 2). It is important to note that the activation of NiBr₂·diglyme (10 mol%) requires 20 mol% of PhMe₂SiZnI. The other nickel catalysts including NiCl₂, Ni(acac)₂ and NiBr₂bpy afforded 5a in only 29%, 66% and 21% yields, with the hydrolyzed acid 3a being formed as the major byproduct (entries 3–5). To our surprise, the hydrated and air-stable Ni(OAc)₂·4H₂O afforded the cross-coupled product 5a in 86% yield (entry 6). A library of ligands was also screened: a simple bipyridine caused a significant reduction in the yield (entry 8), and TMEDA and dppe gave poor yields (entries 9 and 10). The non-polar toluene was not compatible (entry 11). A remarkable improvement in yield to 95% was obtained in DME (entry 12), although the dielectric constant (polarity) and coordinating ability of DME do not significantly vary from those of THF.

Pleasingly, the reaction can be performed at room temperature without a compromise in the yield (entry 13). Interestingly, 5 mol% of Ni(OAc)₂·4H₂O afforded the cross-coupled 5a in 86% isolated yield (entry 14). A further decrease in the loading of catalyst (2 mol%) decreased the yield of 5a (entry 15). When Ni(COD)₂ was employed as a catalyst, 1.5 eq. of carboxylic acid 3a was sufficient to obtain excellent yield (entry 16). Virtually no cross-coupled product 5a was observed in the absence of Ni(OAc)₂·4H₂O (entry 17). Notably, (PhMe₂Si)₂Zn^{8a,h} and PhMe2SiZnCl8j reagents prepared from silyllithium were found to be incompatible and product 5a was observed in only 23% yield (entry 18); the dissolved LiCl may be at play. The detrimental effect of LiCl was confirmed by the addition of 1 eq. of LiCl to the standard reaction that significantly reduced the yield (entry 19). To expand the synthetic utility, we also conducted the reaction on a 4.2 mmol scale using 5 mol% of $Ni(OAc)_2 \cdot 4H_2O$ and obtained **5a** in 80% isolated yield (entry 20). We also found that the mode of addition is critical to obtain a consistent result; PhMe₂SiZnI must be added dropwise at the end of sequential addition, and a change in the sequence resulted in a significant loss of yield.

Having identified the optimal reaction conditions (Table 2, entry 14), we proceeded to examine the scope of carboxylic acids. The primary alkyl carboxylic acids 3a-3g including the long-chain alkyl carboxylic acid afforded the cross-coupled products 5a-5g in good to excellent yields. The α -branched

secondary alkyl carboxylic acids 3h-3i had no impact on the efficiencies and afforded the corresponding acylsilanes 5h-5i in very good yields. Aryl carboxylic acids 3j-3no including π extended naphthalene-2-carboxylic acid 3k and alkenyl carboxylic acids 30-3q were also compatible, affording the corresponding acylsilanes in good yields. The moderate yield concerning 5bc, 5m, 5mn and 5r-5u can be attributed to the incomplete reaction, as we observed a significant amount of PhMe₂SiH at the end of the reaction. We have also observed traces of the decarbonylated byproduct during the synthesis of acylsilanes 5mn, 5no, 5p, 5r and 5t-5u. Various functional groups such as ethers (3a, 3n, 3no, and 3s), alkyl/aryl bromides (3e and 3mn), chloride 3s and medicinally relevant fluoride 3m were tolerated, affording the corresponding cross-coupled products in good to high yields. Carbonyls did not impede the reactivity of silylzinc reagents; ester 3f, ketone 3u and amide 3s were compatible, despite their moderate yields. The O-tosyl protecting group 3g was also compatible. The structurally complex API substances did not impede the reaction; indomethacin 3s, probenecid 3t, anti-inflammatory drug ibuprofen 3r, and ketoprofen 3u afforded the corresponding silylated products 5r-5u. As we observed lower yields on a few substrates,

Table 2 Optimization^a

Entry	Deviation from the above	Temp., time	5a ^a (%)
1	NiBr₂·diglyme, THF	45 °C, 4 h	60 ^c
2	NiBr₂·diglyme, THF	60 °C, 4 h	92
3	NiCl ₂ , THF	60 °C, 4 h	29^d
4	Ni(acac) ₂ , THF	60 °C, 4 h	66
5	NiBr ₂ bpy, THF	60 °C, 4 h	21
6	THF	60 °C, 4 h	86
7	20 mol% of CuI or CuCN	60 °C, 4 h	2
8	bpy instead of dtbpy, THF	60 °C, 4 h	70^d
9	TMEDA instead of dtbpy, THF	60 °C, 4 h	28^d
10	dppe instead of dtbpy, THF	60 °C, 4 h	10
11	Toluene	60 °C, 4 h	38
12	None	60 °C, 4 h	95
13	None	rt, 12 h	90
14	5 mol% Ni(OAc) ₂ ·4H ₂ O	rt, 12 h	94 (86) ^f
15	2 mol% Ni(OAc) ₂ ·4H ₂ O	rt, 12 h	52
16	$Ni(COD)_2$ (1.5 eq. 3a), THF	rt, 12 h	95
17	Without Ni(OAc)2 · 4H2O	rt, 12 h	2
18	Silylzinc from PhMe ₂ SiLi	rt, 12 h	23
19	1 eq. LiCl additive	rt, 12 h	42
20	4.2 mmol of 2a	rt, 12 h	(80)

^a Reaction conditions: 0.39 mmol of **3a**, 0.234 mmol of PhMe₂SiZnI·TMEDA **2a** (0.66 M in toluene), 0.0195 mmol of Ni(OAc)₂·4H₂O and dtbpy, 0.17 M (overall concentration). Isolated acid-chloride **4a** was used in entries 1–7 and 17–19; *in situ* acid-chloride **4a** was used in entries 8–16 and 20. ^b Yield determined by ¹H NMR using 1,3,5-trimethoxy benzene as an internal standard. ^c 1.3 eq. of PhMe₂SiZnI. ^d Incomplete reaction; unreacted starting material was observed in the crude NMR. ^e 1.0 eq. of PhMe₂SiZnI was used. ^f Reactions were repeated at least 10 times throughout the project. DME: 1,2-dimethoxy ethane, yield in parentheses is isolated yield.

we needed to design a complementary copper catalysis to obtain an increased yield. In place of $Ni(OAc)_2 \cdot 4H_2O$, we employed catalytic CuI along with LiCl additive, which resulted in higher yields for substrates 5m and 5u. For substrate 5r, a dual system incorporating both $Ni(OAc)_2 \cdot 4H_2O$ and CuI resulted in a significant increase in yield $(40\% \ vs. \ 89\%)$.

Importantly, the reaction is also compatible with Me₃SiZnI 2b, affording the widely used TMS derived acylsilanes 7 in good to excellent yields. It was necessary to increase the loading of the catalyst to 10 mol% to improve the yield. Similar to PhMe₂SiZnI 2a, Me₃SiZnI 2b was also an efficient reagent (Table 4): primary and secondary alkyl carboxylic acids 3a-3i with various functional groups afforded the cross-coupled products 7a-7i in good to excellent yields. Aryl and vinyl carboxylic acids 3j-3q were also compatible to yield the corresponding acylsilanes 7j-7q in good yields. The API derivatives 7r-7u were also silvlated albeit in lower to moderate yields. In addition, the sterically hindered tertiary alkyl carboxylic acid 3ij afforded acylsilane 7ij in lower yield; an incomplete reaction and decarbonylative protonation may account for the lower yield. Both Ni(OAc)2·4H2O and Ni(COD)2 afforded the acylsilane 7ij in similar yields. N-Tosyl protected isonipecotic acid 3hi was compatible affording the acylsilane 7hi in 58% isolated yield. In general, aryl carboxylic acids gave traces of decarbonylated products and increasing the reaction temperature further increased the undesired decarbonylative silvlation. It is worth noting that the decarbonylation can generate catalytically inactive $L_nNi(CO)_x$ species.³⁵ Additionally, copper catalysis was employed to improve the yield of product 7m. Importantly, the dual Ni(OAc)2/CuI catalytic system significantly improved the yields for substrates 7r and 7u. Gram-scale synthesis of acylsilanes 5e (3.5 mmol), 7a (5 mmol), and 7e (4 mmol) was promising with 82%, 70% and 76% isolated yields. Additional screening using Ni(COD)2 and anhydrous Ni(OAc)2 was done for the low yielding substrates, but no further improvement was observed.

A hypothetical mechanism is shown in Fig. 3. When $Ni(OAc)_2$ was exposed to Me_3SiZnI or $PhMe_2SiZnI$, we observed the formation of disilane with the concomitant formation of a low valent nickel complex, **I**. It has been reported in the literature that the use of organozinc reagents in cross-coupling reactions can lead to either $Ni(0)^{12b,36}$ or $Ni(1)^{37}$ intermediate complexes.

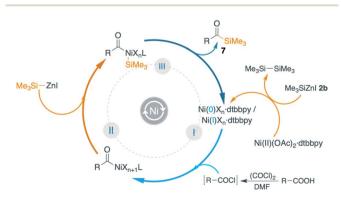


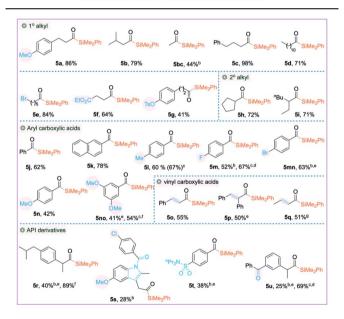
Fig. 3 Mechanistic hypothesis.

The low valent nickel complex **I** undergoes oxidative addition with the *in situ* generated acid chloride to generate the intermediate complex **II**. Subsequent transmetallation to intermediate **III** and reductive elimination affords the acylated product 5 or 7 while regenerating the active catalyst **I**.

In Tables 2-4, the silylzinc reagents 2a and 2b were employed as 0.68 M and 0.56 M solutions, respectively. While studying the stability of these reagents, we discovered that they are quite stable in the form of a solid. To study the general applicability of this new solid Me₃SiZnI 2b, we performed a wide range of organic transformations and the results are summarized in Fig. 4. Initially, both branched and linear allylsilanes 8b and 9b were synthesized through allylation. In the presence of catalytic CuCN, allyl chloride 8a was treated with 2b to generate the branched allylated product 8b in 73% isolated yield. 8g,38 Using allylic alcohol 9a in the presence of a nickel catalyst, the linear silane 9b was likewise produced in 69% yield as a single isomer.8d,39 Because aryl silanes are commonly used in synthetic applications,40 we employed 2b in a nickel-mediated crosscoupling process of aryl bromide 10a, which resulted in the synthesis of aryl silane 10b in 70% isolated yield.41 Crosscoupling of a 2°-alkyl bromide and PhMe₂SiZnCl was recently

Table 3 Cross-coupling with PhMe₂SiZnI^a

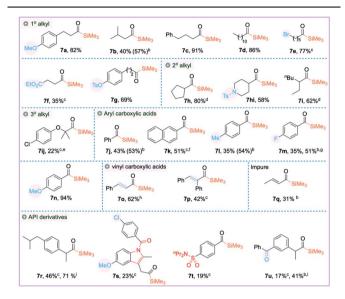
i. (COCl)₂ (3.0 eq.)
DMF (20 mol%), DCM
ii. Ni(OA)₂, 4H₂0 (5 mol%)
3 tdbpy (5 mol%)
R = alkyl/aryl/alkenyl
PhMe_SIZn1 (1.1 eq.)
Br. ti. 2b, her. ti. 2b, her.



^a Reaction conditions: 2 eq. of 3, 1.1 eq. of PhMe₂SiZnI·TMEDA 2a (0.66 M in toluene), 5 mol% of Ni(OAc)₂·4H₂O, 5 mol% of dtbpy, 1,2-dimethoxy ethane (0.17 M). ^b Unreactive PhMe₂SiZnI·TMEDA was observed as PhMe₂SiH. ^c NMR yield. ^d Conditions: 2 eq. of 3, 1 eq. of PhMe₂SiZnI·TMEDA (0.71 M in toluene), 20 mol% of CuI, 1 eq. of LiCl, 1,2-dimethoxy ethane (0.15 M overall concentration), 0 °C − rt. ^eA decarbonylative byproduct was observed. ^f 10 mol% Ni(OAc)₂·4H₂O, 10 mol% 1,10-phen, and 20 mol% of CuI were added. ^g The Brook rearrangement was observed.

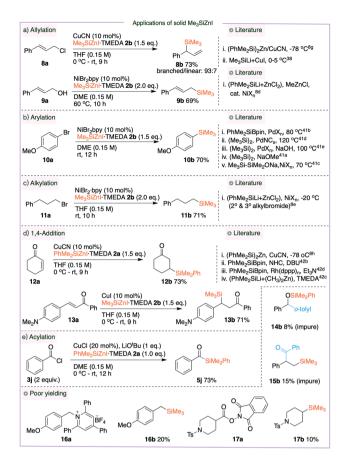
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Table 4 Cross-coupling with Me₃SiZnI^a



^a 2 eq. of 3; 1.2 eq. of Me₃SiZnI·TMEDA 2b (0.56 M in toluene, 1.19 mmol); 10 mol% Ni(OAc)₂·4H₂O; 10 mol% dtbpy; 1,2-dimethoxy ethane (0.17 M). ^b NMR yield. ^c A decarbonylative byproduct was observed. d Dimerization of 3 to a diketone was observed. Ni(COD)2 (10 mol%) instead of Ni(OAc)2 · 4H2O. f Decomposition on silica was observed. g Conditions: 2 eq. of 3, 1eq. of PhMe2SiZnI·TMEDA (0.71 M in toluene), 20 mol% of CuI, 1 eq. of LiCl, 1,2-dimethoxy ethane (0.15 M overall concentration), 0 $^{\circ}$ C - rt. h 6 mmol of 2b was employed. 10 mol% Ni(OAc)2 · 4H2O, 10 mol% 1,10-phen, 20 mol% of CuI was added.

realized,8e and we were ecstatic to see that the new reagent 2b was effective in undergoing the cross-coupling reaction with 1°alkyl bromide 11a, yielding the alkyl silane 11b in a 71% isolated yield. Fortunately, the copper-mediated 1,4-addition of 2a and 2b with enones 12a and 13a yielded the β-silyl ketones 12b and 13b in 73% and 71% isolated yields, respectively.8h,42 Acylsilane 5j was also synthesized by coupling of acid chloride 3j and 2a in the presence of CuCl. We also employed 2a in a novel Brook-rearrangement/cross-coupling of benzaldehyde and bromoarene;43 however, 14b was observed in poor yield. A similar result was obtained in a multi-component reaction between styrene, acid chloride and 2b to yield product 15b.44 Pyridinium salt 16a and redox ester 17a underwent cross-coupling reactions with 2b to afford alkyl silanes 16b and 17b in only 20% and 10% isolated yields respectively, indicating the need for dedicated studies. Samples of solid Me₃SiZnI 2b were stored at three different temperatures (rt, 4 °C and −23 °C) for a period of two months and subjected in the cross-coupling of 10a to afford the aryl silane 10b. The silylzinc 2b samples stored at 4 °C and -23 °C were equally effective as the freshly prepared reagent; however, Me₃SiZnI (two different batches) stored at room temperature gave poor yield (ESI S52†). It is worth noting that Apeloig and Zhivotovskii et al. described the synthesis of solid



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[(Me₃Si)₃Si]₂Zn (stored in a glovebox),⁴⁵ which was later used in silylzincation of alkynes.46

Conclusions

In summary, for the first time, we have developed a method for direct synthesis of silylzinc reagents from silyl iodides and their structures were confirmed by single-crystal XRD. Unlike the use of pyrophoric silyllithium in the synthesis of silylzinc reagents, the current method offers a simplified direct method to access them from silvl halides. The absence of dissolved lithium/magnesium salts in these reagents could be beneficial for various chemical processes. We have also demonstrated the practical synthesis of acylsilanes from unactivated alkyl acid chlorides by nickel, copper and dual catalysis. The methodology is compatible with various functional groups, and accommodates sterically hindered secondary and tertiary alkyl carboxylic acids. Structurally complex and API molecules are also silvlated conveniently. The general synthetic utility of these reagents is shown in a broad range of reactions. Further study to expand the synthetic scope of these reagents is currently underway in our laboratory.

Author contributions

The manuscript was written through the contributions of all authors. R. C., F. T. P. and K. S. performed the experiments. All authors have approved the final version of the manuscript.

Conflicts of interest

The authors declare no competing financial interest.

Acknowledgements

We acknowledge financial support from the Science and Engineering Research Board, Ramanujan Fellowship SB/S2/RJN059/2015, CSIR (Council of Scientific and Industrial Research, 02(0409)/21/EMR-II) and IISER Trivandrum. RC acknowledges CSIR, FTP acknowledges IISER Trivandrum and KS acknowledges DST-Inspire for fellowships.

Notes and references

- 1 (a) A. Franz and S. Wilson, J. Med. Chem., 2013, 56, 388; (b) P. L. Fuchs, Handbook of Reagents For Organic Synthesis, Reagents For Silicon-Mediated Organic Synthesis, John Wiley & Sons, 2011; (c) Y. Apeloig, The Chemistry of Organic Silicon Compounds, Wiley, 1989.
- 2 (a) Y. Minami and T. Hiyama, Chem.-Eur. J., 2019, 25, 391; (b) S. Bähr, W. Xue and M. Oestreich, ACS Catal., 2019, 9, 16; (c) M. Oestreich, E. Hartmann and M. Mewald, Chem. Rev., 2013, 113, 402; (d) L. Xu, L. Li, G. Lai and J. Jiang, Chem. Soc. Rev., 2011, 40, 1777; (e) T. H. Chan and D. Wang, Chem. Rev., 1992, 92, 995; (f) P. Xiao, L. Gao and Z. Song, Chem.-Eur. J., 2019, 25, 2407; (g) A. Hameed, R. D. Alharthy, J. Iqbal and P. Langer, Tetrahedron, 2016, 72, 2763; (h) M. Greenhalgh, Iron-catalysed hydrosilylation of alkenes and alkynes, Springer International Publishing, Cham, 2016, p. 33; (i) M. D. Greenhalgh, A. S. Jones and S. P. Thomas, *ChemCatChem*, 2015, 7, 190; (j) B. M. Trost and Z. T. Ball, Synthesis, 2005, 2005, 853; (k) M. G. Voronkov, V. M. Dyakov and S. V. Kirpichenko, J. Organomet. Chem., 1982, 233, 1; (l) I. Beletskaya and C. Moberg, Chem. Rev., 2006, 106, 2320; (m) M. A. Brook, Silicon in Organic, Organometallic, and Polymer Chemistry, Wiley, New York, 2000.
- 3 (a) J. P. Morken, in *Comprehensive Organic Synthesis II*, 2014, p. 939; (b) I. Beletskaya and C. Moberg, *Chem. Rev.*, 1999, 99, 3435; (c) M. B. Ansell, O. Navarro and J. Spencer, *Coord. Chem. Rev.*, 2017, 336, 54; (d) M. Suginome and Y. Ito, *J. Chem. Soc., Dalton Trans.*, 1998, 1925; (e) M. Suginome and Y. Ito, *Chem. Rev.*, 2000, 100, 3221.
- 4 (a) T. Ohmura and M. Suginome, Bull. Chem. Soc. Jpn., 2009,
 82, 29; (b) J.-J. Feng, W. Mao, L. Zhang and M. Oestreich,
 Chem. Soc. Rev., 2021, 50, 2010.
- 5 (a) S. Díez-González and S. P. Nolan, Acc. Chem. Res., 2008,
 41, 349; (b) B. Marciniec, Comprehensive Handbook on Hydrosilylation, Pergamon, 1992; (c) B. Marciniec, Hydrosilylation, Springer, 2008; (d) B. Marciniec and J. Guliński, J. Organomet. Chem., 1993, 446, 15; (e)
 Y. Nakajima and S. Shimada, RSC Adv., 2015, 5, 20603; (f)
 A. K. Roy, in Adv. Organomet. Chem., Elsevier, 2007, p. 1; (g)
 J. L. Speier, in Catalysis and Organic Syntheses: Advances in Organometallic Chemistry, Elsevier, 1979, p. 407.

- 6 A. P. Cinderella, B. Vulovic and D. A. Watson, J. Am. Chem. Soc., 2017, 139, 7741.
- 7 J. Duan, K. Wang, G. L. Xu, S. Kang, L. Qi, X. Y. Liu and X. Z. Shu, Angew. Chem., Int. Ed., 2020, 59, 23083.
- 8 (a) M. Oestreich, G. Auer and B. Weiner, Synthesis, 2006, 2006, 2113; (b) A. Hensel and M. Oestreich, Chem.-Eur. J., 2015, 21, 9062; (c) Y. Y. Kong and Z. X. Wang, Adv. Synth. Catal., 2019, 361, 5440; (d) B. Yang and Z.-X. Wang, Org. Lett., 2019, 21, 7965; (e) C. Chu, Y. Liang and G. Fu, J. Am. Chem. Soc., 2016, 138, 6404; (f) C. Fopp, E. Romain, K. Isaac, F. Chemla, F. Ferreira, O. Jackowski, M. Oestreich and A. Perez-Luna, Org. Lett., 2016, 18, 2054; (g) D. Vyas and M. Oestreich, Chem. Commun., 2010, 46, 568; (h) M. Oestreich and B. Weiner, Synlett, 2004, 2139; (i) L. Zhang and M. Oestreich, Org. Lett., 2018, 20, 8061; (f) H. Azuma, K. Okano and H. Tokuyama, Chem. Lett., 2011, 40, 959.
- 9 Y. Morizawa, H. Oda, K. Oshima and H. Nozaki, *Tetrahedron Lett.*, 1984, 25, 1163.
- 10 (a) C. K. Hazra and M. Oestreich, Org. Lett., 2012, 14, 4010;
 (b) A. Perez-Luna, M. Oestreich, C. Fopp, K. Isaac,
 E. Romain, F. Chemla, F. Ferreira and O. Jackowski,
 Synthesis, 2017, 49, 724.
- 11 (a) W. C. Still, *J. Org. Chem.*, 1976, **41**, 3063; (b) E. Yamamoto, S. Ukigai and H. Ito, *Synlett*, 2017, **28**, 2460.
- 12 (a) P. Knochel, M. Schade, S. Bernhardt, G. Manolikakes, A. Metzger, F. Piller, C. Rohbogner and M. Mosrin, Beilstein J. Org. Chem., 2011, 7, 1261; (b) X. Wu, X. Li, W. Huang, Y. Wang, H. Xu, L. Cai, J. Qu and Y. Chen, Org. Lett., 2019, 21, 2453; (c) D. Wang, H. Niu, M. Xie, G. Qu, H. Wang and H. Guo, Org. Lett., 2014, 16, 262; (d) S. J. Edeson, E. J. M. Maduli, S. Swanson, P. A. Procopiou and J. P. A. Harrity, Eur. J. Org. Chem., 2016, 2016, 83; (e) A. Krasovskiy, V. Malakhov, A. Gavryushin and P. Knochel, Angew. Chem., Int. Ed., 2006, 45, 6040; (f) C. Feng, D. Cunningham, Q. Easter and S. Blum, J. Am. Chem. Soc., 2016, 138, 11156.
- 13 (a) X. Wang, F. Liu, Y. Li, Z. Yan, Q. Qiang and Z. Q. Rong, *ChemCatChem*, 2020, 12, 5022; (b) H.-J. Zhang, D. L. Priebbenow and C. Bolm, *Chem. Soc. Rev.*, 2013, 42, 8540; (c) G. Boyce, S. Greszler, J. Johnson, X. Linghu, J. Malinowski, D. Nicewicz, A. Satterfield, D. Schmitt and K. Steward, *J. Org. Chem.*, 2012, 77, 4503; (d) W. H. Moser, *Tetrahedron*, 2001, 57, 2065; (e) P. C. B. Page, S. S. Klair and S. Rosenthal, *Chem. Soc. Rev.*, 1990, 19, 147; (f) A. G. Brook, *Acc. Chem. Res.*, 1974, 7, 77.
- 14 (a) J. Feng and M. Oestreich, Angew. Chem., Int. Ed., 2019, 58, 8211; (b) J. Rong, R. Oost, A. Desmarchelier, A. Minnaard and S. Harutyunyan, Angew. Chem., Int. Ed., 2015, 54, 3038; (c) J. González, J. Santamaría and A. Ballesteros, Angew. Chem., Int. Ed., 2015, 54, 13678; (d) R. Lettan, C. Galliford, C. Woodward and K. Scheidt, J. Am. Chem. Soc., 2009, 131, 8805; (e) R. B. Lettan, T. E. Reynolds, C. V. Galliford and K. A. Scheidt, J. Am. Chem. Soc., 2006, 128, 15566.
- 15 (a) J. R. Schmink and S. W. Krska, J. Am. Chem. Soc., 2011,133, 19574; (b) S. Ramgren and N. Garg, Org. Lett., 2014,16, 824.

Edge Article

16 (a) X. Lu, J. Zhang, L. Xu, W. Shen, F. Yu, L. Ding and G. Zhong, *Org. Lett.*, 2020, 22, 5610; (b) M. Sasaki, Y. Kondo, T. Moto-ishi, M. Kawahata, K. Yamaguchi and K. Takeda, *Org. Lett.*, 2015, 17, 1280; (c) Y. Matsuya, K. Wada, D. Minato and K. Sugimoto, *Angew. Chem., Int. Ed.*, 2016, 55, 10079; (d) M. Decostanzi, J. Godemert, S. Oudeyer, V. Levacher, J.-M. Campagne and E. Leclerc, *Adv. Synth. Catal.*, 2016, 358, 526; (e) J.-H. Ye, L. Quach, T. Paulisch and F. Glorius, *J. Am. Chem. Soc.*, 2019, 141(41), 16227; (f) B. Huang, M. Wei, E. Vargo, Y. Qian, T. Xu and F. D. Toste, *J. Am. Chem. Soc.*, 2021, 143, 17920; (g) C. Stuckhardt, M. Wissing and A. Studer, *Angew. Chem., Int. Ed.*, 2021, 60, 18605.

- 17 (a) D. Priebbenow, J. Org. Chem., 2019, 84, 11813; (b) F. Tang, P.-J. Ma, Y. Yao, Y.-J. Xu and C.-D. Lu, Chem. Commun., 2019, 55, 3777; (c) H. J. Zhang, P. Becker, H. Huang, R. Pirwerdjan, F. F. Pan and C. Bolm, Adv. Synth. Catal., 2012, 354, 2157; (d) K. Ito, H. Tamashima, N. Iwasawa and H. Kusama, J. Am. Chem. Soc., 2011, 133, 3716; (e) M. Sasaki, Y. Kondo, M. Kawahata, K. Yamaguchi and K. Takeda, Angew. Chem., Int. Ed., 2011, 50, 6375; (f) J. Chen, C. Ding, W. Liu, X. Hou and L. Dai, J. Am. Chem. Soc., 2010, 132, 15493; (g) R. Unger, F. Weisser, N. Chinkov, A. Stanger, T. Cohen and I. Marek, Org. Lett., 2009, 11, 1853; (h) S. N. Greszler and J. S. Johnson, Org. Lett., 2009, 11, 827; (i) R. Lettan, C. Woodward and K. Scheidt, Angew. Chem., Int. Ed., 2008, 47, 2294; (j) Y. Obora, Y. Ogawa, Y. Imai, T. Kawamura and Y. Tsuji, J. Am. Chem. Soc., 2001, 123, 10489; (k) K. Takeda, M. Fujisawa, T. Makino, E. Yoshii and K. Yamaguchi, J. Am. Chem. Soc., 1993, 115, 9351; (l) H. J. Reich, J. J. Rusek and R. E. Olson, J. Am. Chem. Soc., 1979, 101, 2225; (m) A. G. Brook, J. Am. Chem. Soc., 1958, 80, 1886; (n) N. Lee, C.-H. Tan and D. Leow, Asian J. Org. Chem., 2019, 8, 25.
- 18 (a) K. Jahyo, L. Jae Hyoung, K. Koan Seong, J. Jae Uk and P. Chongsuh, *Tetrahedron Lett.*, 1987, 28, 3261; (b) J. P. Picard, R. Calas, J. Dunogues, N. Duffaut, J. Gerval and P. Lapouyade, *J. Org. Chem.*, 1979, 44, 420; (c) I. Fleming and U. Ghosh, *J. Chem. Soc., Perkin Trans.* 1, 1994, 257; (d) A. Capperucci, A. Degl'Innocenti, C. Faggi, A. Ricci, P. Dembech and G. Seconi, *J. Org. Chem.*, 1988, 53, 3612; (e) B. F. Bonini, M. Comes-Franchini, G. Mazzanti, U. Passamonti, A. Ricchi and P. Zani, *Synthesis*, 1995, 1995, 92.
- 19 (a) K. Yamamoto, S. Suzuki and J. Tsuji, *Tetrahedron Lett.*, 1980, **21**, 1653; (b) K. Yamamoto, A. Hayashi, S. Suzuki and J. Tsuji, *Organometallics*, 1987, **6**, 974.
- 20 F. Geng and R. E. Maleczka Jr, *Tetrahedron Lett.*, 1999, 40, 3113.
- 21 (a) B. Wu and R. Zhu, ACS Catal., 2020, 10, 510; (b) X. Deng,
 G. Zhou, J. Tian and R. Srinivasan, Angew. Chem., Int. Ed.,
 2020, 22, 7024.
- 22 A. Kunai, T. Sakurai, E. Toyoda, M. Ishikawa and Y. Yamamoto, *Organometallics*, 1994, **13**, 3233.
- 23 (a) L. Zhu, R. M. Wehmeyer and R. D. Rieke, *J. Org. Chem.*, 1991, **56**, 1445; (b) E. Erdik, *Tetrahedron*, 1987, **43**, 2203.
- 24 M. S. Newman and F. J. Evans, J. Am. Chem. Soc., 1955, 77, 946.

- 25 (a) G. Picotin and P. Miginiac, J. Org. Chem., 1987, 52, 4796;(b) J. K. Gawroński, Tetrahedron Lett., 1984, 25, 2605.
- 26 S. Huo, Org. Lett., 2003, 5, 423.
- 27 (a) K. Takagi, Chem. Lett., 1993, 22, 469; (b) K. Takagi,
 Y. Shimoishi and K. Sasaki, Chem. Lett., 1994, 23, 2055; (c)
 R. F. Abdulla, Aldrichimica Acta, 1988, 21, 31.
- 28 M. Bellassoued, M. Gaudemar, A. El Borgi and B. Baccar, *J. Organomet. Chem.*, 1985, **280**, 165.
- 29 R. Goddard, C. Krüger, N. A. Ramadan and A. Ritter, *Angew. Chem.*, *Int. Ed.*, 1995, **34**, 1030.
- 30 V. Murugesan, V. Balakrishnan and R. Rasappan, *J. Catal.*, 2019, 377, 293.
- 31 T. N. Majid and P. Knochel, Tetrahedron Lett., 1990, 31, 4413.
- 32 K. Takagi, N. Hayama and S. Inokawa, *Bull. Chem. Soc. Jpn.*, 1980, 53, 3691.
- 33 (a) C. Gosmini, M. Amatore, S. Claudel and J. Périchon, Synlett, 2005, 2171; (b) I. Kazmierski, C. Gosmini, J.-M. Paris and J. Périchon, Tetrahedron Lett., 2003, 44, 6417.
- 34 (a) D. S. Ziegler, K. Karaghiosoff and P. Knochel, Angew. Chem., Int. Ed., 2018, 57, 6701; (b) M. Balkenhohl,
 D. Ziegler, A. Desaintjean, L. Bole, A. Kennedy, E. Hevia and P. Knochel, Angew. Chem., Int. Ed., 2019, 58, 12898.
- 35 C. A. Malapit, J. R. Bour, S. R. Laursen and M. S. Sanford, *J. Am. Chem. Soc.*, 2019, **141**, 17322.
- 36 (a) J. Hu, H. Wu, C. Li, W. Sheng, Y. Jia and J. Gao, *Chemistry*, 2011, 17, 5234; (b) R. Jana, T. Pathak and M. Sigman, *Chem. Rev.*, 2011, 111, 1417.
- 37 (a) G. Schwarzwalder, C. Matier and G. Fu, Angew. Chem., Int. Ed., 2019, 58, 3571; (b) R. Soler-Yanes, I. Arribas-Álvarez, M. Guisán-Ceinos, E. Buñuel and D. J. Cárdenas, Chem.–Eur. J., 2017, 23, 1584; (c) A. Oelke, J. Sun and G. Fu, J. Am. Chem. Soc., 2012, 134, 2966; (d) V. Phapale, E. Buñuel, M. García-Iglesias and D. Cárdenas, Angew. Chem., Int. Ed., 2007, 46, 8790; (e) G. Jones, J. Martin, C. McFarland, O. Allen, R. Hall, A. Haley, R. Brandon, T. Konovalova, P. Desrochers, P. Pulay and D. Vicic, J. Am. Chem. Soc., 2006, 128, 13175.
- 38 J. G. Smith, S. E. Drozda, S. P. Petraglia, N. R. Quinn, E. M. Rice, B. S. Taylor and M. Viswanathan, *J. Org. Chem.*, 1984, 49, 4112.
- 39 R. Moser, T. Nishikata and B. H. Lipshutz, *Org. Lett.*, 2009, **12**, 28.
- 40 (a) L. T. Ball, M. Green, G. C. Lloyd-Jones and C. A. Russell, Org. Lett., 2010, 12, 4724; (b) L. T. Ball, G. C. Lloyd-Jones and C. A. Russell, Chem.-Eur. J., 2012, 18, 2931; (c) J. Xie, K. Sekine, S. Witzel, P. Krämer, M. Rudolph, F. Rominger and A. S. K. Hashmi, Angew. Chem., Int. Ed., 2018, 57, 16648; (d) K. Gondo, J. Oyamada and T. Kitamura, Org. Lett., 2015, 17, 4778; (e) M. J. Harper, E. J. Emmett, J. F. Bower and C. A. Russell, J. Am. Chem. Soc., 2017, 139, 12386; (f) W. E. Brenzovich, J.-F. Brazeau and F. D. Toste, Org. Lett., 2010, 12, 4728; (g) M. Shibata, H. Ito and K. Itami, J. Am. Chem. Soc., 2018, 140, 2196; (h) K. Funaki, T. Sato and S. Oi, Org. Lett., 2012, 14, 6186.
- 41 (a) A. Postigo and R. A. Rossi, Org. Lett., 2001, 3, 1197; (b)
 H. Guo, X. Chen, C. Zhao and W. He, Chem. Commun.,
 2015, 51, 17410; (c) K. Hitoshio, H. Yamagishi,

J. Shimokawa and H. Yorimitsu, *Chem. Commun.*, 2021, 57, 6867; (*d*) T. Nagata, T. Inoue, X. Lin, S. Ishimoto, S. Nakamichi, H. Oka, R. Kondo, T. Suzuki and Y. Obora, *RSC Adv.*, 2019, **9**, 17425; (*e*) E. Shirakawa, T. Kurahashi, H. Yoshida and T. Hiyama, *Chem. Commun.*, 2000, 1895.

Chemical Science

- 42 (a) G. Auer and M. Oestreich, Chem. Commun., 2006, 311; (b)
 J. M. O'Brien and A. H. Hoveyda, J. Am. Chem. Soc., 2011, 133, 7712; (c)
 A. Vaughan and R. D. Singer, Tetrahedron Lett., 1995, 36, 5683; (d)
 C. Walter, G. Auer and M. Oestreich, Angew. Chem., Int. Ed., 2006, 45, 5675; (e)
 T. Kitanosono, L. Zhu, C. Liu, P. Xu and S. Kobayashi, J. Am. Chem. Soc.,
- 2015, 137, 15422; (f) K.-s. Lee and A. H. Hoveyda, J. Am. Chem. Soc., 2010, 132, 2898.
- 43 M. Takeda, K. Yabushita, S. Yasuda and H. Ohmiya, *Chem. Commun.*, 2018, **54**, 6776.
- 44 D. Ni and M. K. Brown, ACS Catal., 2021, 11, 1858.
- 45 R. Dobrovetsky, Y. Kratish, B. Tumanskii, M. Botoshansky, D. Bravo-Zhivotovskii and Y. Apeloig, *Angew. Chem., Int. Ed.*, 2012, 51, 4671.
- 46 E. Romain, K. Vega-Hernández, F. Guégan, J. Sanz García, C. Fopp, F. Chemla, F. Ferreira, H. Gerard, O. Jackowski, S. Halbert, M. Oestreich and A. Perez-Luna, *Adv. Synth. Catal.*, 2021, 363, 2634.